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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,979	10/28/2003	Pierre Aman	Strom.7309	4425

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EXAMINER

WHALEY, PABLO S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 07/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/694,979	<b>Applicant(s)</b> AMAN ET AL.	
	<b>Examiner</b> Pablo Whaley	<b>Art Unit</b> 1631	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 01 May 2006.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 6-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                                                                               |                                                                                         |
|-----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                                                   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                                          | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/28/2003</u> | 6) <input type="checkbox"/> Other: _____                                                |

## **DETAILED ACTION**

### *APPLICANT'S ELECTION*

Applicant's election of Group I (claims 1-5) in the reply filed on 5/1/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 6-20 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim.

### *CLAIMS UNDER EXAMINATION*

Claims 1-5 are currently under examination.

### *INFORMATION DISCLOSURE STATEMENT*

The information disclosure statement filed 10/28/2003 has been considered in full.

### **VAGUE AND INDEFINITE**

Claim 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "registering the number of amplification cycles." It is unclear as to the intended meaning of "registering" in this context, as it is unclear with what the amplification cycles are "registered" with (i.e. a database, a program, a graph, etc.). Clarification is requested. Claims 2-5 are rejected as they depend directly from instant claim 1.

Claim 2 recites the limitation "the two reactions." There is lack of antecedent basis for this limitation. Parent claim 1 recites only see ONE CPR (reaction). It is unclear if applicant intends amplification of each nucleic acid (e.g. each dilution) to be a separate reaction. Correction is requested.

Claim 3 recites the limitation "such as." Regarding claim 3, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 3 recites the limitation the procedure of claim 1 "or an equivalent procedure." The term "equivalent" is a relative term of degree, therefore it is unclear as to the intended meaning of an "equivalent procedure." Clarification is requested. Furthermore, if it is an "equivalent procedure", then claim 3 is not dependent on claim 1 and one skilled in the art would not know what method steps are intended for claim 3. Clarification is again requested.

Claim 3 recites the limitation a ratio of two nucleic acids "is determined." It is unclear if this is intended to be an active method step or an intended result of the method. If applicant intends for this to be an intended result, then it is noted that an intended result does not, in fact,

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limit the method of claim 1. If an active method step is intended, then claim 2 should recite active, positive verbs. Clarification is requested.

Claim 3 recites the limitation CT values "are measured" and PCR efficiencies "are determined." It is unclear if these are intended to be active method steps (i.e. actual claim limitations) or are intended to further limit the data. Clarification is requested. It is noted that as written, the measurement and determination may occur before the intended method is to be performed, and therefore these steps do not, in fact, limit the method at all.

Claim 3 recites the limitation "a training set of...samples." It is unclear in what way the recitation of a "training set" limits the claimed method. Confusingly, neither claim 1 nor claim 3 recites comparison to a training set, and the equation of claim 3 does not require any data from the measurement of the training set. Furthermore, neither of the two nucleic acids to be included in the ratio of claim 3 is limited to be one from a training set. Clarification is requested.

Claim 4 recites the limitation "the two PCR assays." There is lack of antecedent basis for this limitation. Parent claim 1 recites only see ONE CPR (reaction). It is unclear if applicant intends amplification of each nucleic acid (e.g. each dilution) to be a separate reaction. Correction is requested.

Claim 4 recites the limitation "also taking into account...relative sensitivity." It is unclear whether "taking into account" is referring to the an active method step or referring to a limitation of the equation recited in claim 4. If applicants intend for this to be an active method step, it is unclear in what way the relative sensitivity is taken into account, as one usually assumes the "sensitivity" is the same if the same apparatus, labels, etc. are used. Clarification is requested. Furthermore, the recitation of "relative sensitivity" is confusing. As the claims do not recite any difference between the conditions for the different polynucleotides amplified, one skilled in the

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art would not know what "relativity sensitivity" is intended to be "relative" to. Clarification is requested.

Claim 5 recites the limitation "RNA, preferably one or more mRNAs." A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). In the present instance, claim 5 recites the broad recitation "RNA", and the claim also recites "mRNA" which is the narrower statement of the range/limitation. Correction is requested.

Claim 5 recites the limitation "similar process." The term "similar" is a relative term of degree, therefore it is unclear how "similar" a process need to be in order to be considered "similar." Clarification is requested.

## **PRIOR ART**

### **Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1-2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Pfaaf (Nucleic Acids Research, 2001, Vol. 29, No. 9, p.2002-2007)

Pfaaf generally teaches a mathematical model for relative quantitation in real-time RT-PCR. More specifically, Pfaaf et al. teach the following limitations of the instant claimed invention: determination of sample and control copy number and variability using RNA [Table 1], as in instant claims 1 and 5; comparison of PCR efficiencies for reference gene and cDNA sample based on controlled sample dilution [Fig. 1], as in instant claims 1 and 2; a graph of cycle numbers required to obtain certain amounts of product [Fig. 2], which equates to "registering of cycle numbers" as in instant claim 1; and an expression ratio for a target gene based on PCR efficiency and copy number [Equation 1], which if rearranged, becomes the equation recited in instant claim 3.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Meijerink et al. (Journal of Molecular Diagnostics, 2001, Vol. 3, No. 2, p.55-61)

Meijerink et al. generally teach a mathematical method to compensate for different amplification efficiencies between patient DNA samples using QRT-PCR [Abstract]. More specifically, Meijerink et al. teach the following limitations of the instant claimed invention: comparison of PCR efficiency using template dilutions and patient samples [Table 2], as in instant claim 1; DNA or RNA [p. 56, Col. 1, ¶ 4], as in instant claims 1 and 5; a graph of cycle numbers required to obtain certain amounts of product [Fig. 1], which equates to "registering of cycle numbers" as in instant claim 1; a correction factor (i.e. dilution factor) [p.57, Equation 6]; equations for normalization of the target PCR to a reference PCR [p. 56, Col. 1, ¶ 4] and ratios

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of nucleic acids in a sample [Equations 2 and 5], and variables [Table 1], as in instant claims 3 and 4. It is noted that  $C_1$  and  $C_2$  are constants that are being divided (i.e.  $C_1 / C_2$ ), which equates to  $K_{RS}$  as in instant claim 4.

### CONCLUSION

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley

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MARJORIE A. MORAN  
PRIMARY EXAMINER

*Marjorie A. Moran*  
7/24/06